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## Angiogenesis induced by the implantation of self-bone marrow cells: a new material for therapeutic angiogenesis.

Hamano K, Li TS, Kobayashi T, Kobayashi S, Matsuzaki M, Esato K.

First Department of Surgery, Yamaguchi University School of Medicine, Ube, Japan. kimikazu@po.cc.yamaguchi-u.ac.jp

Bone marrow, contains various primitive cells that are thought to secrete several angiogenic growth factors and may also differentiate into endothelial cells. The present study was conducted to investigate the possibility that bone marrow cells could be a novel material to induce angiogenesis. The expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in rat bone marrow cells was examined by immunohistochemistry. The production of VEGF was compared in tissue culture supernatant under the conditions of normoxia and hypoxia. The process of angiogenesis that occurred following the implantation of bone marrow cells was determined using a rat cornea model. VEGF- and bFGF-positive cells were found in rat bone marrow. The production of VEGF from bone marrow cells was significantly more enhanced by hypoxic conditions than by normoxic conditions. The rat cornea model showed that bone marrow cell implantation created new vessels. The implantation of self-bone marrow cells is a novel and simple method of inducing angiogenesis.

PMID: 10972343 [PubMed - indexed for MEDLINE]

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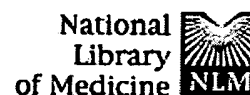
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## Bone marrow-derived endothelial progenitor cells for vascular regeneration.

Murayama T, Asahara T.

Division of Cardiovascular Research, St Elizabeth's Medical Center of Boston, Brighton, MA 02135-2997, USA.

It has recently been demonstrated that postnatal neovascularization is not restricted to angiogenesis, but also includes vasculogenesis. During adult vasculogenesis, bone marrow (BM)-derived endothelial progenitor cells (EPCs) are recruited to the systemic circulation in response to certain cytokines and/or tissue ischemia, and incorporate into sites of neovascularization. EPCs have also been investigated as therapeutic agents in a 'supply-side' approach to promoting neovascularization under pathological conditions. This review highlights the discovery of BM-derived EPCs and their therapeutic potential for vascular regeneration.

Publication Types:

- Review
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PMID: 12222878 [PubMed - indexed for MEDLINE]

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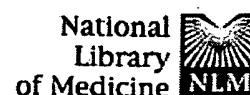
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☐ 1: Nat Med 1999 Apr;5(4):434-8

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**Ischemia- and cytokine-induced mobilization of bone marrow-derived endothelial progenitor cells for neovascularization.****Takahashi T, Kalka C, Masuda H, Chen D, Silver M, Kearney M, Magner M, Isner JM, Asahara T.**

Department of Medicine (Cardiology), St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, Massachusetts 02135-2997, USA.

Endothelial progenitor cells (EPCs) have been isolated from circulating mononuclear cells in human peripheral blood and shown to be incorporated into foci of neovascularization, consistent with postnatal vasculogenesis. We determined whether endogenous stimuli (tissue ischemia) and exogenous cytokine therapy (granulocyte macrophage-colony stimulating factor, GM-CSF) mobilize EPCs and thereby contribute to neovascularization of ischemic tissues. The development of regional ischemia in both mice and rabbits increased the frequency of circulating EPCs. In mice, the effect of ischemia-induced EPC mobilization was demonstrated by enhanced ocular neovascularization after cornea micropocket surgery in mice with hindlimb ischemia compared with that in non-ischemic control mice. In rabbits with hindlimb ischemia, circulating EPCs were further augmented after pretreatment with GM-CSF, with a corresponding improvement in hindlimb neovascularization. There was direct evidence that EPCs that contributed to enhanced corneal neovascularization were specifically mobilized from the bone marrow in response to ischemia and GM-CSF in mice transplanted with bone marrow from transgenic donors expressing beta-galactosidase transcriptionally regulated by the endothelial cell-specific Tie-2 promoter. These findings indicate that circulating EPCs are mobilized endogenously in response to tissue ischemia or exogenously by cytokine therapy and thereby augment neovascularization of ischemic tissues.

PMID: 10202935 [PubMed - indexed for MEDLINE]

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